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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,676	09/14/2001	Christine Libon	PF98PCTSEQ/dln	9130

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EXAMINER
ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/01/2003

6

DOCKETED

Response Due / RR
October 1, 2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/936,676	LIBON ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-72* is/are pending in the application.

4a) Of the above claim(s) *36,37 and 55-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,35,38-54 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *34-72* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I in Paper No. 5 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The amendment filed on 4-23-2003 is acknowledged. Claims 34-35 and 38-54 have been amended. Claim 72 has been added. Claims 34-5, 38-54 and 72 are currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-35, 38-54 and 72 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34 and 72 are rendered vague and indefinite by the use of the term "orienting". It is unclear what is meant by said term. Is Applicant claiming that the administration of the antigen and the *Klebsiella* membrane fraction results in a Th1 or mixed immune response? If so, it is suggested that the phrase "A method of inducing a Th1 type and or mixed Th1/Th2 type immune response directed against an antigen or hapten..." be used in claim 34 and the phrase "which is effective in inducing a Th1 type and or mixed Th1/Th2 type immune response directed against an antigen or hapten..." be used in claim 72.

Claims 34 and 72 are rendered vague and indefinite by the use of the phrase "in which the Th1 response is close to or greater than the Th2 type response". It is unclear what is meant by said phrase. What criteria are being used to compare the types of response? What constitutes being close? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 38 recites improper Markush language. Proper language would be "the antigen or hapten is selected from the group consisting of antigens or haptens specific to an infectious agent and an antigen associated with a tumor cell" or "the antigen or hapten is an antigen or hapten specific to an infectious agent or an antigen associated with a tumor cell".

Claim 39 is difficult to interpret since Applicant uses the function of the *Klebsiella* membrane fraction (i.e. inducing a Th1 response directed to the antigen) to define the antigen. As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 41 is rendered vague and indefinite by the use of the term "capable of". There is a difference between having the means to perform a function and actually performing said function. It is unclear whether the binding of the "complex" to mammalian serum albumin is meant to be a limitation of the recited claim.

Claim 42 is rendered vague and indefinite by the use of the term "derived from". It is unclear what is meant by said term. What constitutes a derivative? What processes are considered derivations? How much divergence can said derivative have from the wild type G protein?

Claims 43 and 48 are rendered vague and indefinite by the use of the term "genetic recombination. It is unclear how a proteinaceous complex can result from a process limited to genetic material.

Claim 46 is rendered vague and indefinite by the use of the phrase "introduced into at least one of the compounds contained in the membrane fraction and/or in the antigen...". It is unclear how a linking element can be put "into" an antigen or how an internalized element can link to another entity.

Claim 49 is rendered vague and indefinite by the term "carry the membrane fraction...in a form...which makes it possible to enhance..." It is unclear what is meant by said term. Does the addition of the agent change the physical and chemical properties of the antigen, hapten or complex? If so, what is changed?

Claims 49 and 53 are rendered vague and indefinite by the use of the phrase "makes it possible". Said term is interpreted in the same manner as "capable of" and therefore, it is unclear whether "enhancing the stability or immunogenicity of the antigen..." (claim 49) and "regulation of the immune response" (claim 53) are meant to be limitations of the recited claims.

Claim 51 recites improper Markush language. Moreover, it is unclear what is meant by the term "a particle of **the** liposome, microsphere or nanosphere type or any type of structure allowing the encapsulation...". What constitutes a particle of a liposome, microsphere or nanosphere? Why are said compositions referred to a "structures"? As written, it is impossible to determine the metes and bounds of the claimed invention.

Regarding claims 52 and 54, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 52 and 54 recite improper Markush language. It is suggested that the "selected from the group consisting of a, b, and c" format be used.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 34, 38-40, 44, 48 and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Rauly et al. (Research in Immunology, Vol 149 No. 1, page 99, Jan 1998).

The instant claims are drawn to methods of inducing a Th1 or mixed Th1/Th2 type response against an antigen utilizing *Klebsiella pneumonia* membrane fractions combined (bound) with an antigen wherein said antigen if from an infectious agent or is associated with tumor cells. Moreover, said membrane fraction/antigen complexes may be recombinantly produced and may be part of pharmaceutical compositions.

Rauly et al. disclose the use compositions comprising the outer membrane protein A (OmpA) of *Klebsiella pneumoniae* as an immunopotentiator (carrier/adjuvant). Said protein was recombinantly produced and coupled to a B-cell epitope derived from the respiratory syncytial virus. The resulting complex (rP40-G1) induces a mixed Th1/Th2 response when administered to animals.

Claims 34, 38-41, 43-45, 48-49 and 72 are rejected under 35 U.S.C. 102(e) as being anticipated by Binz et al. (U.S. Patent 6,197,929).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claims are drawn to methods of inducing a Th1 or mixed Th1/Th2 type response against an antigen utilizing *Klebsiella pneumonia* membrane fractions combined (or

covalently bound) with an antigen wherein said antigen if from an infectious agent or is associated with tumor cells. Moreover, said membrane fraction/antigen complexes may be recombinantly produced, may further comprise peptide/protein that can bind mammalian serum albumin and may be part of pharmaceutical compositions.

Binz et al. disclose the use compositions comprising the outer membrane protein A (OmpA) of *Klebsiella pneumoniae* as an immunopotentiator (carrier/adjuvant). Said protein was recombinantly produced and coupled to protein G of the respiratory syncytial virus (RSV) [see column 3, lines 25-32). Said conjugates may be coupled either covalently or recombinantly [see column 3, lines 9-19] and may further comprise a peptide/protein that can bind mammalian serum albumin [see column 3, lines 20-25] and can be used in pharmaceutical compositions comprising pharmaceutically acceptable excipients [see column 3, lines 49-54]. The disclosed membrane fraction protein:antigen complex (P40-Ext) was disclosed to induce a Th1 response when administered to animals as exemplified by the production of a highly quantitative delayed hypersensitivity response [see column 9, lines 35-41] and macrophage activation [see column 9, lines 50-55].

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Binz et al. (WO 96/14415).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Robert A. Zeman
June 30, 2003